Original Article

Blood transfusion is associated with increased resource utilisation, morbidity and mortality in cardiac surgery

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ABSTRACT

The purpose of the present investigation was to examine the impact of blood transfusion on resource utilisation, morbidity and mortality in patients undergoing coronary artery bypass graft (CABG) surgery at a major university hospital. The resources we examined are time to extubation, intensive care unit length of stay (ICULOS) and postoperative length of stay (PLOS). We further examined the impact of number of units of packed red blood cells (PRBCs) transfused during PLOS.

This is a retrospective observational study and includes 1746 consecutive male and female patients undergoing primary CABG (on- and off-pump) at our institution. Of these, 1067 patients received blood transfusions, while 677 did not. The data regarding the demography, blood transfusion, resource utilisation, morbidity and mortality were collected from the records of patients undergoing CABG over a period of three years. The mean time to extubation following surgery was 8.0 h for the transfused group and 4.3 h for the nontransfused group ($P \leq 0.001$). The mean ICULOS for the transfused group was 1.6 d and 1.2 d for the nontransfused group ($P < 0.001$). The PLOS was 7.2 d for the transfused group and 4.3 d for no-transfused cohorts ($P \leq 0.001$). In all patients and in patients with no preoperative morbidity, partial correlation coefficients were used to examine the effects of transfusion on mortality, time to extubation, ICULOS and PLOS. Linear regression model was used to assess the effect of number of PRBC units transfused on PLOS. We noted that PLOS increased with the number of PRBCs units transfused. Transfusion is significantly correlated with the increased time to extubation, ICULOS, PLOS and mortality. The transfused patients had significantly more postoperative complications than their nontransfused counterparts ($P \leq 0.001$). The 30-day hospital mortality was 3.1% for the transfused group with no deaths in the nontransfused group ($P \leq 0.001$).

We conclude that the CABG patients receiving blood transfusion have significantly longer time for tracheal extubation, ICULOS, PLOS and higher morbidity and 30-day hospital mortality. Blood transfusion was an independent predictor of increased resource utilisation, postoperative morbidity and mortality.

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INTRODUCTION

Blood transfusion is common in patients undergoing coronary artery bypass graft (CABG) surgery. Approximately 20% of the available blood supply in the United States is consumed by patients undergoing cardiac surgery.[1] It is expected that with the increase in age and comorbidities among patients presenting for surgery, blood transfusion will further increase.[2] Despite this, there is a relatively scant information with regard to the impact of transfusion on resource utilisation and postoperative morbidity and mortality. The goal of our investigation was to examine the impact of transfusion on the duration of intubation, intensive care unit length of stay (ICULOS), postoperative length of stay (PLOS), morbidity and mortality in patients undergoing CABG surgery. We also examined

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the relation between the number of units of packed red blood cells (PRBCs) transfused and PLOS in this group of patients.

MATERIALS AND METHODS

This study was approved by the institutional review board for collecting data from the patient's medical records. This is a retrospective observational study. The study population included all patients undergoing primary CABG at a tertiary care heart centre over a period of three years. There were a total of 1746 patients. All patients underwent CABG surgery through a median sternotomy incision. Aspirin was discontinued 7 d prior to elective surgery.

One day before surgery, the patients in the hospital were premedicated with morphine and scopolamine prior to their arrival in the operating room. Patients arriving on the day of surgery were premedicated with midazolam as deemed appropriate by the anaesthesiologist. Intraoperative monitors included the standard American Society of Anesthesiologists monitors along with 5-lead electrocardiogram with continuous automated ST segment analysis, continuous arterial pressure determination using a radial artery catheter and a pulmonary artery catheter. All patients received standard fast-track anaesthetic induction using a combination of 5-10 μg/kg fentanyl and 0.05-0.1 mg/kg midazolam. We used 0.1 mg/kg vecuronium or 1 mg/kg rocuronium for neuromuscular blockade. Anaesthesia was maintained with supplements of propofol, isoflurane or sevoflurane as deemed appropriate by the anaesthesiologist. Patients undergoing CABG under CPB received 300 units/kg of heparin, and the activated clotting time (ACT) was maintained above 400 s prior to institution of cardiopulmonary bypass. Patients undergoing off-pump coronary artery bypass (OPCAB) received 100 to 200 units/kg of heparin to maintain the ACT above 350 s. Both groups received additional heparin as deemed necessary to maintain the ACT at the desired levels. The left internal mammary artery was harvested as surgically indicated and the saphenous vein was used for additional conduits. Patients undergoing CABG under cardiopulmonary bypass (CPB) were cannulated with an aortic cannula and a two-stage venous cannula prior to institution of cardiopulmonary bypass. Membrane oxygenators were used in all patients. Both retrograde and antegrade intermittent cold (6 ºC) blood cardioplegia solution was administered for myocardial protection. Systemic temperature was permitted to maintain at 30-32 ºC during cardiopulmonary bypass. All distal and proximal anastomoses were constructed using a single cross-clamp technique. In patients undergoing OPCAB, special off-pump coronary retractors and stabilisers were utilised during distal coronary anastomosis (Guidant, Indianapolis, IN). Proximal anastomoses were constructed using multiple cross-clamp technique. All patients were actively rewarmed to 37 ºC prior to weaning from CPB. All patients undergoing CABG under CPB received epsilon aminocaproic acid during surgery. No antifibrinolytics were used in the OPCAB patients. The guidelines we followed for blood transfusion was triggered by the hematocrit values, ventricular function and other associated comorbidities. The end points of blood transfusion were to maintain a hematocrit value over 25% in patients with normal haemodynamics and ventricular function and over 30% in patients with compromised haemodynamics and ventricular function. These guidelines applied to all patients.

All demographic and clinical data were collected on the standardized data collection forms as required by the New York State cardiac surgical reporting system for predicting the risk-adjusted mortality rate according to the New York State department of health. This included age, gender, weight, body surface area (BSA), use of intraaortic balloon pump, left ventricular ejection fraction, use of cardiopulmonary bypass pump, number of distal coronary grafts, comorbid conditions such as diabetes, hypertension, congestive heart failure (CHF), renal failure, chronic obstructive pulmonary disease (COPD), previous myocardial infarction and postoperative bleeding requiring reoperation. The data pertaining to pre- and post-operative hematocrit values, the time to postoperative tracheal extubation, PRBC transfusion, ICULOS, PLOS and mortality and morbidity were obtained from the medical records of the patients. Extubation time is defined as the time from leaving the operating room to the removal of the endotracheal tube. ICULOS is defined as the time of admission to the ICU until the time of discharge to the intermediate care or step down unit. PLOS is defined as the time from the day of surgery until the day of discharge from the hospital. All patients were assessed for extubation within the first hour of arrival in the ICU and placed on our standard extubation protocol. The data pertaining to postoperative complications such as stroke, renal failure and 30-day mortality were also collected.

Statistical methods

Data are summarized and described using means, standard deviations and proportions. The demographic,

clinical and outcome variables were compared between the transfused and nontransfused patients using the Wilcoxon rank sum test. The *P* values for these comparisons are reported. A *P* value of <0.05 was considered significant. Partial correlation coefficients and linear and logistic regression analysis were used for assessing the relations between the key outcome variables and clinical correlates. All the values have been expressed as mean ± standard deviation (SD).

RESULTS

The demographic and clinical data are presented in Table 1. A total of 1746 patients participated in this study. Of the 1746 patients, 1069 received blood transfusion, while 677 did not. The number of females was significantly higher in the transfused group; these patients were significantly older in age, smaller in size with slightly lower ejection fractions. Transfused patients demonstrated significantly lower pre- and postoperative hematocrit values. Moreover, significantly higher incidence of preoperative hypertension, diabetes, myocardial infarction, renal insufficiency, congestive heart failure (CHF) and chronic obstructive pulmonary disease (COPD) and peripheral vascular disease (PVD). They also exhibited a higher incidence of mammary artery usage and postoperative bleeding requiring reexploration. The transfused patients demonstrated a significantly higher incidence of postoperative renal failure, neurological complications, infection and mortality. No deaths occurred among the patients of the nontransfused group as compared to 3.1% among the transfused group. These data are displayed in Table 2.

Table 1: Demographic and clinical data

	Nontransfused	Transfused	*P* value
No. of patients	677	1069	
No. of females	96	382	<0.001
Age (years)	60.8 ± 10.4	67.0 ± 11.0	<0.001
Weight (Kg)	92.1 ± 18.1	80.5 ± 17.9	<0.001
BSA (m^2)	2.0 ± 0.2	1.9 ± 0.2	<0.001
Ejection fraction (%)	47.5 ± 12.1	45.8 ± 12.6	0.006
Diabetes (%)	29.5	34.2	0.041
Hypertension (%)	63.4	69.3	<0.010
Preoperative renal failure (%)	0.6	4.4	<0.001
Prior MI (%)	23.2	22.6	NS
Prior CVA (%)	4.6	10.1	<0.001
COPD (%)	8.7	14.0	<0.001
PVD (%)	11.5	21.6	<0.001
CHF (%)	8.7	21.1	<0.001
Preoperative Hct	37.5 ± 3.8	33.3 ± 4.4	<0.001
Postoperative Hct	33.0 ± 3.8	30.5 ± 3.4	<0.001

MI: myocardial infarction; CVA: cerebrovascular accident; COPD: chronic obstructive pulmonary disease; PVD: peripheral vascular disease; CHF: congestive heart failure; Hct: hematocrit; NS: not significant; and BSA: body surface area

The mean time for tracheal extubation was 8.0 h for the transfused group and 4.3 h for the nontransfused group ($P < 0.001$). The transfused group also had significantly more patients who required >72 h of mechanical ventilation ($P < 0.001$). The mean ICULOS was 1.6 versus 1.2 d for the nontransfused group ($P < 0.001$). The mean PLOS was 7.2 d for the transfused group and 4.2 d for the nontransfused group ($P < 0.001$). Resource utilisation and mortality data are displayed in Table 3. The *P* values for partial correlation coefficients between transfusion and time to extubation, ICULOS, PLOS and mortality were <0.001. We further examined the correlation between transfusion and time to extubation, ICULOS and PLOS in patients with no prior illness and found the *P* values to be <0.05. Partial correlations were adjusted for the effects of age, sex and body surface area (BSA). These results are displayed in Tables 4 and 5. Linear

Table 2: Surgical data

	Nontransfused	Transfused	*P* value
No. of distal grafts			
Internal mammary artery use (%)	39.8	60.2	<0.001
Duration of CPB (min)	96.5 ± 24.9	106.1 ± 31.8	<0.001
Cross-clamping time (min)	71.8 ± 19.8	76.3 ± 25.4	0.013
Intraaortic balloon (%)	26.9	73.1	0.001
Bleeding requiring reexploration (%)	0	4.1	<0.001
Postoperative renal failure	0	1.1	0.005
Acute dialysis (%)			
Postoperative CVA (%)	0.4	2.2	0.004
Postoperative infection (%)	1.0	1.4	<0.001
Postoperative GI complication (%)	0	1.1	0.005
Mortality (%)	0	3.1	<0.001

CPB: cardiopulmonary bypass; CVA: cerebrovascular accident; GI: gastrointestinal; and NS: not significant

Table 3: Resource utilisation data

	Nontransfused	Transfused	*P* value
Time to extubation (h)	4.3 ± 4.6	8.0 ± 7.5	<0.001
Ventilation >72 h (%)	0	3.6	<0.001
ICULOS (days)	1.2 ± 0.7	1.6 ± 1.6	<0.001
PLOS (days)	4.3 ± 2.0	7.2 ± 6.8	<0.001

ICULOS: intensive care unit length of stay and PLOS: postoperative length of stay

Table 4: Partial correlation coefficients* and *P*-values for all data (*n* = 1746)

	Transfusion	Red blood cells
Mortality	0.079 (0.001)	0.383 (<0.001)
Extubation	0.218 (<0.001)	0.259 (<0.001)
PLOS	0.199 (<0.001)	0.434 (<0.001)
ICULOS	0.136 (<0.001)	0.209 (<0.001)

*Partial correlation coefficients are the correlation coefficients adjusted for possible confounders. The coefficients are adjusted for effects of age, sex and body surface area. ICULOS: intensive care length of stay and PLOS: postoperative length of stay

Table 5: Partial correlation coefficients* and *P*-values for patients with no prior illness (*n* = 263)

	Transfusion	Red blood cells
Mortality	-	-
Extubation	0.227 (<0.001)	0.133 (0.030)
PLOS	0.145 (0.018)	0.628 (<0.001)
ICULOS	0.165 (0.007)	0.266 (<0.001)

*Partial correlations are adjusted for effects of age, sex and body surface area. ICULOS: intensive care length of stay and PLOS: postoperative length of stay

regression model was used to examine the impact of the number of units of PRBCs transfused on PLOS in all patients and in patients with no prior comorbidities. These results are shown in Figures 1 and 2.

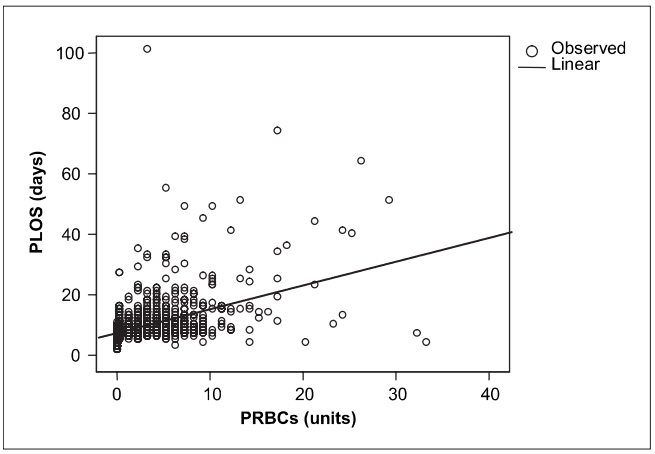

Figure 1: Relation between the postoperative length of stay (PLOS) and number of units of PRBCs received.
Circles represent the raw data. The line represents a statistically significant linear regression; *P*<0.001. PLOS =3.90 ±0.82x PRBCs***. ***This is a linear regression equation expressing PLOS as a function of the number of units of PRBCs in all patients. PRBCs: Packed red blood cells and PLOS: Post operative length of stay

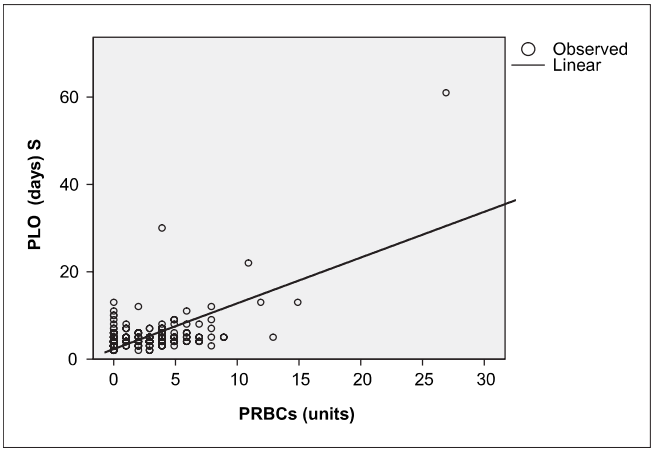

Figure 2: Relation between the postoperative length of stay (PLOS) and number of units of PRBCs received in patients with no preoperative morbidity (This figure shows the PLOS and number of units of PRBCs transfused in patients with no preoperative comorbidities such as MI, DM, HTN, CHF and renal failure) Circles represent the raw data. The line represents a statistically significant linear regression; *P*<0.001. PLOS =3.21 ±1.05x PRBCs***. ***This is a linear regression equation expressing PLOS as a function of the number of units of PRBCs in patients with no preoperative comorbidities. PRBCs: Packed red blood cells and PLOS: Post operative length of stay

DISCUSSION

The goal of the present investigation was to examine the impact of blood transfusion on resource utilisation, morbidity and mortality in patients undergoing elective CABG surgery in our tertiary care heart center. The resources examined were time to extubation, ICU LOS and PLOS. The significant findings of this study are that the transfused patients remained intubated for prolonged duration and had significantly longer ICULOS and PLOS as compared to their nontransfused counterparts. The transfused patients also had higher incidence of postoperative neurological and gastrointestinal (GI) complications, renal failure and infection. They also exhibited a higher incidence of postoperative bleeding requiring reexploration. The transfused patients had significantly higher incidence of 30-day mortality as compared to their nontransfused cohorts.

The first resource we examined was the duration of intubation and mechanical ventilation after surgery. Our results showed that the transfused patients were intubated for significantly longer time as compared to nontransfused patients. This data is in agreement with previously published reports.[3,4] Our data also showed that 3.6% of the transfused patients remained intubated for longer than 72 h; however, in the nontransfused group, no patient remained intubated for longer than 72 h. This is an important utilisation factor because early tracheal extubation has been shown to decrease the cost of surgery.[5] We examined ICULOS as the subsequent resource. We believe that this resource generally follows a trend similar to the time to extubation. Our data shows that the transfused patients had significantly longer ICULOS similar to that in extubation. This fact is in agreement with those from previous reports.[3-7] With regard to PLOS, the transfused patients had significantly longer PLOS as compared to their nontransfused cohorts. Our results are in agreement with those of previous reports.[3,6,7] Our study shows that the incidence of postoperative complications was significantly higher in the transfused group. They had a significantly higher incidence of postoperative renal failure, stroke, infection and GI complications[3,8,9] and were reexplored for postoperative bleeding more often. This data is in agreement with previously reported studies.[8,10] We examined the 30-day mortality and found that patients who received blood transfusion had significantly higher incidence of 30-day mortality. No deaths occurred in the nontransfused group. Previous studies have examined mortality in the transfused CABG patients and a majority of these reports have documented the deleterious effects

of transfusion on long-term mortality. Our results are in agreement with those of previous studies.[7,8,10-12] We further examined the relationship between the number of units of PRBCs transfused and PLOS. We found that PLOS increased as the number of units of blood administered increased in a linear fashion. The length of stay increased by approximately 0.82 d for every unit of blood transfused. This is in agreement with a previously published report examining the relation between PLOS and number of units of PRBCs transfused.[6]

It is important to note that our transfused patients were older, smaller and had lower preoperative hematocrit values. The transfused group comprised significantly more females. All these are the known risk factors for transfusion.[2,13,14] The transfused group also had significantly more preoperative comorbidities. They had a significantly higher incidence of preoperative diabetes, hypertension, renal failure, CHF, COPD and PVD. They also had a lower preoperative hematocrit value. This is similar to what has been reported in previous studies.[8,10] The question is "is it the higher incidence of preoperative comorbidities that is responsible for the increased incidence of postoperative morbidity and mortality or is transfusion a marker for the severity of illness." Our analysis shows that transfusion is an independent predictor of increased resource utilisation because even in patients with no preoperative morbidities, transfusion correlated with increased duration of intubation, ICULOS and PLOS. Among these patients, PLOS increased with the number of units of PRBCs transfused. Some of the previous reports have encountered the same question and have concluded that transfusion is an independent predictor of early and late mortality and increased ICULOS and PLOS.[3,4,6] Our results are in agreement with these previous reports.

In conclusion, our data show that patients who received transfusion had significantly longer time to extubation, ICULOS and PLOS. They also had significantly higher incidence of the 30-day mortality. We found that PLOS increased with the number of units of PRBCs transfused.

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